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EXAMINER	
SOUAYA, JEHANNE E	
ART UNIT	PAPER NUMBER
1655	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/672,221	Boyle et al
Examiner	**Art Unit**
Jehanne Souaya	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 4, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above, claim(s) *1-9, 14-24, and 26-30* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *10-13 and 25* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-30* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election to the restriction requirement of 05/02/2001 of Group III, claims 10-13, 21-23, and 25, SEQ ID NOS 3,4 and 6-17, is acknowledged. Upon further review, the examiner has set forth a further restriction requirement to these elected claims:

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

III. Claims 10-13 and 25, drawn to polypeptides, classified in class 530, subclass 350.

VI. Claims 21-23, drawn to methods for detecting polypeptides and to methods for identifying compounds that bind to polypeptides, classified in class 435, subclass 7.1.

Brief description of Groups outlined in the previous office action of 5/2/01 (see previous office action for a detailed description of each group):

I. Claims 1-9, 14-16, 18-20, and 24 drawn to polynucleotides.
II. Claims 26-28 drawn to nucleic acid arrays.
IV. Claim 17 drawn to antibodies.
V. Claims 29-30 drawn to methods of treating.

The inventions are distinct, each from the other because of the following reasons:

Regarding the invention of Group III:

3. As set forth in the previous restriction requirement, the invention of group III is patentably distinct from the inventions of groups I and IV as they are drawn to patentably distinct products (see section 3 of Office Action mailed 5/2/01). The invention of group III is patentably distinct from the invention of group II as the inventions are unrelated (see section 4 of Office

action mailed 5/2/01). The invention of group III is patentably distinct from the invention of group V (see section 5 of 5/2/01 office action)as the method of treatment of Group V is unobvious over the polypeptides of Group III and further the polypeptides of Group III can be used to make fusion proteins.

4. The inventions of Groups III and VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide of group III can be used to make fusion proteins.

Regarding the invention of Group VI:

5. The inventions of Groups VI and I, II, & V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions of Groups I and II are not used in the methods of Group VI. Furthermore, the inventions of Groups V and VI are not usable together as one is directed to detecting a polypeptide or a compound that binds a polypeptide while the method of group V is directed to methods of treatment. The methods of Groups V and VI have different modes of operation.

6. The inventions of Groups VI and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the method of Group VI can be carried out using a ligand that binds to the polypeptide in the method of Group VI, that is materially different, structurally and functionally, than an antibody of Group IV.

7. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

9. During a telephone conversation with Ivor Elrifi on November 6, 2001 a provisional election was made without traverse to prosecute the invention of Group III, claims 10-13 and 25. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-9, 14-24, and 26-30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. **An action on the merits for Claims**

10-13 and 25, SEQ ID NOS 4 and 6-17, follows. SEQ ID NO 3 has not been examined as it is a polynucleotide, which is directed to the non elected invention of Group I.

Priority

10. Applicant's claim for priority to applications 09/560,875, filed 4/27/2000, and 09/496,914, filed 2/3/2000, is acknowledged. However, the currently pending claims, 10-13, and 25, have not been awarded the benefit of the earlier filing date of either application as the subject matter in the claims is not disclosed in either the '875 or the '914 applications.

Claim Rejections - 35 USC § 101

Definitions: **[from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]**

"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the specific and substantial tests (see below).

"Specific Utility" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example,

both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. ' 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility."

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a specific or substantial utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. ' 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial asserted utility would be considered to be met.

A "Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.
See also the MPEP at 2107 - 2107.02.

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claims 10-13 and 25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claims encompass isolated polypeptides that are at least 80% identical to SEQ ID NOS 4 and 6-17, to the translated protein coding portion thereof, the mature protein coding portion thereof, the extracellular portion thereof, or the active domain thereof. The claims further encompass polypeptides that have LRR protein like activity that comprise at least five or at least 10 consecutive amino acids of the polypeptide sequence from the group consisting of SEQ ID NOS 4 and 6-17. The specification teaches that SEQ ID NO 4 is predicted to be encoded by the nucleic acid of SEQ ID NO 3, and that SEQ ID NO 17 is the mature form of SEQ ID NO 4. The specification teaches that SEQ ID NO 15 is a signal peptide which is located at positions 1-18 of SEQ ID NO 4 and is the extracelluar portion of SEQ ID NO 4 [see p. 117-119]. The specification further teaches that 9 Leucine Rich Repeats (LRR) were predicted to be present in SEQ ID NO 4 and correspond to SEQ ID NOS 6-14. The specification, however, does not teach the biological activity or function of SEQ ID NOS 4 or 17 or where "active domains" are located. The specification asserts that the signal peptide, SEQ ID NO 15, and the predicted transmembrane portion, SEQ ID NO 16, have use on their own, but teaches that this use(which is not disclosed in the specification) must be confirmed by expression in mammalian cells (see pp 117-118) and sequencing of the cleaved product (in the case of SEQ ID NO 15, p. 117, lines 26-27). Leucine rich repeats are generally known to be involved in protein protein interactions, however a large class of proteins exist which contain leucine rich repeats, having a wide range of functions (see Kobe and Deisenhofer, 1995 and analysis below), therefore the prediction of putative leucine rich

repeats in SEQ ID NO 4 would not indicate to one of skill a specific or substantial utility for the claimed polypeptides.

The specification asserts the following uses for the claimed polypeptides: at page 7, lines 10-15, the specification teaches that the polypeptides can be used a) to generate an antibody that specifically binds the polypeptide, b) as molecular weight markers, and c) as food supplements. The specification further asserts that the claimed polypeptides can be used as potential therapeutics in the treatment of heart failure, nerve injury, insulin and non insulin dependent diabetes, muscle disorders, tumor growth, stress syndromes, inflammation, blood clotting, immune function, and bleeding disorders. (p. 7, lines 20-29). At pages 49-50 (bridging paragraph), the specification teaches that the polypeptides can also be used in assays to determine biological activity or levels of protein in biological fluids, and also to isolate correlative receptors or ligands. The claimed polypeptides, however, are not supported by a specific asserted utility because the disclosed uses of the polypeptides are not specific and are generally applicable to any polypeptide. These are non-specific uses that are applicable to polypeptides in general and not particular or specific to the polypeptide being claimed.

Further, the claimed polypeptides are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, a polypeptide can be used to obtain an antibody. The antibody could then be used in conducting research to isolate the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only

be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case, none of the antibodies that are to be produced as final products resulting from processes involving claimed polypeptides have specific and substantial utilities. The research contemplated by applicant(s) to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context of use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility of the utility has not been assessed.

It is noted that the specification teaches that SEQ ID NO 4 has 44% similarity and 30% identity to human insulin like growth factor binding protein complex acid labile subunit (ALS), which contains leucine rich repeats. Absent factual evidence, however, a percentage sequence identity of less than 100% is not deemed reasonable to support one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of a similar known biomolecule. Kobe and Deisenhofer (1995, Current Opinion in Structural Biology, 1995, pp 409-416, referred to as "Kobe") teach that known LRR containing proteins have only two things in common: repetitive sequences and involvement in protein protein interactions (see p. 410, col

1 and 2, Fig 2 and table 1). Kobe teaches that LRR proteins take part in a wide range of processes, such as signal transduction, cell adhesion, development, DNA repair, recombination, transcription, and RNA processing, and that recently, it was discovered that some LRR containing proteins can bind non protein ligands. Table 1 illustrates the wide range of functions of LRR containing proteins. Thus, the prediction of putative leucine rich repeats in SEQ ID NO 4 would not indicate to one of skill in the art a specific or substantial utility for the claimed polypeptides as the structural similarities of certain regions of SEQ ID NO 4 to other LRR proteins does not indicate the specific biological function or activity of the claimed polypeptides or to specific diseases that can be identified or treated with the claimed polypeptides. With regard to a use for a single leucine rich repeat, Kobe teaches that a single leucine-rich motif most probably does not fold into a defined structure and that several LRRs appear to jointly form a module and that the function of LRR domains can be modulated by changing the number of repeats with a single domain (see p. 412, col 1).

The specification also teaches that SEQ ID NO 4 also has 45 % similarity and 32% identity to human glycoprotein V protein (see p 117). Bernard-Souleir syndrome, an inherited bleeding disorder, is caused by a lack of functional GP Ib-IX-V complex. It is known for nucleic acids as well as proteins, however, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. (See Russel et al, J. Mol. Biol. Vol. 244, 1994, pp 332-350, who teaches that the

results of an analysis of side chain to side chain secondary structure and accessibility between related proteins suggest that there is little in common between distantly related protein structures and that secondary structure lengths and loops in distantly related structures vary substantially- p. 345). The specification does not teach the biological function or activity of SEQ ID NOS 4 or 6-17. Furthermore, the specification provides no specific or substantial utility as to the use of the claimed polypeptides in therapeutics for bleeding disorders, or more specifically for Bernard Souleir syndrome. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks support regarding utility. Further experimentation would be required of the skilled artisan to determine a use for the polypeptides of the claimed invention. As noted by Brenner v. Manson, 383 US 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use - testing... a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Claim Rejections - 35 USC § 112

Enablement

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-13 and 25 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

14. Claims 10, 11, and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide which comprises an amino acid sequence which is at least 80% identical to the amino acid sequence of SEQ ID NOS 4 and 6-17, to the translated protein coding portion thereof, the mature protein coding portion thereof, and the extracellular portion thereof, does not reasonably provide enablement for an isolated polypeptide that is 80% identical to the active domain of SEQ ID NOS 4 and 6-17. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (See *In re Wands,* 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include, but are not limited to:

Quality of Experimentation Necessary
Amount of Direction and Guidance
Presence and Absence of Working Examples

Nature of the Invention
Level of predictability and unpredictability in the art

The claimed invention is drawn to an isolated polypeptide comprising an amino acid sequence which is at least 80% identical to the active domain of SEQ ID NOS 4, 6-16 or 17. The specification teaches SEQ ID NOS 4 and 6-17. The claimed invention broadly encompasses active domains of the claimed polypeptides as well as variants, mutants, and homologs of the claimed polypeptides. The specification teaches that SEQ ID NO 4 is predicted to be encoded by the nucleic acid sequence of SEQ ID NO 3, nucleotide positions 164 to 2244), (see pp 116-117), thus the examiner interprets the phrase "the translated protein coding portion thereof" to be SEQ ID NO 4. The specification teaches that SEQ ID NO 17 is the mature form of SEQ ID NO 4, thus the examiner interprets the phrase "the mature protein coding portion thereof" to be SEQ ID NO 17. The specification teaches that SEQ ID NO 15 corresponds to nucleotide positions 1-18 of SEQ ID NO 4, which is a signal peptide which corresponds to the extracellular portion of SEQ ID NO 4 [see p. 117, lines 26-28], thus the examiner interprets the phrase "the extracellular portion thereof" to be SEQ ID NO 15. The specification teaches that fragments of the proteins of the present invention which are capable of exhibiting biological activity are encompassed (p. 37, lines 19-22) by the claimed invention, however, the specification does not teach or provide working examples illustrating the biological activity or function of SEQ ID NOS 4, 6-16, or 17, nor does the specification teach which part of SEQ ID NOS 4, 6-16, or 17 have biological activity or are active domains of the claimed polypeptides.

The specification teaches that SEQ ID NO 4 is predicted to contain 9 leucine rich repeats (SEQ ID NOS 6-14), a signal peptide (SEQ ID NO 15), and a transmembrane domain (SEQ ID NO 16) [see pp 116-119]. The specification teaches that SEQ ID NO 4 has 44% similarity and 30% identity to human insulin like growth factor binding protein complex acid labile subunit (ALS), which contains leucine rich repeats. Ueki et al (PNAS, June 6, 2000, vol. 97, pp 6868-6873) teaches that mice, which contain an ALS gene that has been inactivated (see abstract) are observed to exhibit growth deficiencies. Ueki teaches that this mutation replaced the coding region of exon1, intron1, and 1,300 bp of exon 2, resulting in the deletion of the first 435 of the 603 amino acid residues of mouse ALS and 16 of the 19 leucine repeats thought to be essential for ternary complex formation (see p. 6869, col2, "Results"). Absent factual evidence, however, a percentage sequence identity of less than 100% is not deemed reasonable to support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of a similar known biomolecule. Kobe and Deisenhofer (1995, Current Opinion in Structural Biology, 1995, pp 409-416, referred to as "Kobe") teach that known LRR containing proteins have only two things in common: repetitive sequences and involvement in protein protein interactions (see p. 410, col 1 and 2, Fig 2 and table 1). Kobe teaches that LRR proteins take part in a wide range of processes, such as signal transduction, cell adhesion, development, DNA repair, recombination, transcription, and RNA processing, and that recently, it was discovered that some LRR containing proteins can bind non protein ligands. Table 1 illustrates the wide range of functions of LRR containing proteins. Thus, the prediction of putative leucine

rich repeats in SEQ ID NO 4 would not indicate to one of skill in the art a predictable correlation between an active domain in SEQ ID NO 4 and ALS. With regard to the "activity" of a single leucine rich repeat, Kobe teaches that a single leucine-rich motif most probably does not fold into a defined structure and that several LRRs appear to jointly form a module and that the function of LRR domains can be modulated by changing the number of repeats with a single domain (see p. 412, col 1).

Since the specification has not taught the function or biological activity of SEQ ID NO 4, or SEQ ID NO 6-17, which parts of the claimed polypeptides are active domains, or specific function or activity assays that the skilled artisan could use to determine which domains in the claimed polypeptides correspond to "active domains" and the art teaches the unpredictability of correlating structural similarities between LRR proteins and their function, the skilled artisan would be required to perform undue experimentation to make or use polypeptides that are at least 80% identical to the active domains of SEQ ID NOS 4, 6-16 or 17. As stated previously, the specification has not taught the function of the polypeptides of SEQ ID NOS 4, 6-16, or 17 nor has the specification taught where to modify the polypeptide to produce a protein with at least 80% identity to the active domain of SEQ ID NO 4, 6-16 or 17. The skilled artisan would have no way of knowing which polypeptide sequences were "active domains" of the claimed polypeptides because the specification does not provide a description of the amino acid sequences which constitute these "active domains". The instant claims are drawn to undisclosed sequences encoding modifications that have not been contemplated. The skilled artisan would be

required to perform manipulations and extensive modification of the protein to determine where and how to make modifications to determine which fragments of the polypeptide were responsible for it's activity. Due to the lack of guidance from the specification as to which parts of the claimed polypeptides correspond to active domains, these modifications and manipulations would require trial and error, which is considered undue experimentation. Therefore, the skilled artisan would be required to perform undue experimentation to identify any polypeptide which was an active fragment of the claimed polypeptides or to identify any polypeptide which was at least 80% identical to an active fragment of the polypeptides of the presently claimed invention.

Written Description

15. Claims 10-13 and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO: 4 and 6-17- Polypeptides comprising SEQ ID NOS 4 and 17 and polypeptides consisting of the sequences of SEQ ID NOS: 6-16 meet the written description provisions of 35 USC 112, first paragraph. However, claims 10, 11, and 25 are directed to polypeptides that comprise an amino acid sequence that is at least 80% identical to SEQ ID NOS 4, and 6-17, the translated protein coding portion thereof (interpreted to be SEQ ID NO 4, see analysis in section 14 above), the mature protein coding portion thereof (interpreted to

be SEQ ID NO 17), the extracellular portion thereof (interpreted to be SEQ ID NO 15), or the active domain thereof and encompass full length proteins as well as functional fragments, mutated sequences, allelic variants, and splice variants from any species. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Claims 12 and 13 are directed to polypeptides that have LRR protein like activity that comprise at least 5 or 10 consecutive amino acids from the polypeptide sequences selected from the group consisting of SEQ ID NOS 4 and 6-17. This recitation also encompasses full length proteins as well as functional fragments, mutated sequences, allelic variants, and splice variants from any species. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. The teachings of Kobe illustrate that LRR proteins are a diverse class of proteins, and that proteins from this broad genus, while containing certain structural similarities to other LRR proteins, have very different functions. Thus a single sequence from this broad genus is not representative of the functionally different proteins from this broad class. Absent a written description disclosing a representative number of proteins of this broad class of proteins, the specification fails to show that applicant was "in possession of the claimed invention" at the time the application for patent was filed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS: 4, and 6-17, the skilled artisan cannot envision the detailed chemical structure of the encompassed proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

Accordingly, the specification does not provide a written description of the invention of claims 10-13 and 25.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 10-13 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Hardiman et al (WO 98/50545, publication date: November 12, 1998).

Hardiman teaches human toll like receptor proteins DTLR2-DTLR10,which are homologous to Drosophila Toll receptor (see abstract), which contains 22 LRR ectodomains (p. 69). Hardiman teaches the polypeptide sequence of SEQ ID NO 12, which corresponds to DTLR6 (p. 8, p. 125). SEQ ID NO 12, taught by Hardiman, is a polypeptide sequence which comprises an 11 mer (at positions 697-707 of SEQ ID NO 12 taught by Hardiman) that is identical to amino acids 252-262 of SEQ ID NO 4 and amino acids 234-244 of SEQ ID NO 17 of the instant invention. Thus the teachings of Hardiman anticipate the limitations of both claims 12 and 13 as the claims are drawn to a polypeptide that comprises an amino acid sequence having LRR protein like activity which comprises at least 5 or 10 consecutive amino acids from the

polypeptide sequences selected from the group consisting of SEQ ID NO 4, 6-16, and 17. The specification defines the term " LRR protein like activity" as a biological activity that is similar to the biological activity of an LRR protein. Thus a protein that contains leucine rich repeats satisfies the definition of LRR like protein.

SEQ ID NO 12, taught by Hardiman, also comprises an 11mer that is identical to 11 of the 14 amino acid residues of SEQ ID NO 10. Thus SEQ ID NO 12 taught by Hardiman, comprises an amino acid sequence which is at least 80% identical to SEQ ID NO 10 of the instantly claimed invention. Hardiman also specifically teaches compositions comprising the DTLR6 protein and a carrier wherein the carrier is an aqueous compound (p. 10 lines 32-35), thus inherently anticipating the limitations of claim 11. Hardiman further teaches kits (p. 11) comprising the DTLR proteins and polypeptides taught by Hardiman (inherently anticipates the limitations of claim 25).

18. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Miller et al (US Patent 5,298,239; March 29, 1994).

Miller teaches a polypeptide sequence, SEQ ID NO 6, of 610 amino acids where amino acids 81-89 are identical to amino acids 254-262 of SEQ ID NO 4 of the instant invention. Miller anticipates the polypeptides of claim 13 as the claim is drawn to a polypeptide that comprises an amino acid sequence having LRR protein like activity which comprises at least 5 consecutive amino acids from the polypeptide sequences selected from the group consisting of SEQ ID NO 4, 6-16, and 17. The specification defines the term " LRR protein like activity" as a

biological activity that is similar to the biological activity of an LRR protein. SEQ ID NO 6, taught by Miller is the amino acid sequence of wild-type platelet glycoprotein Ib alpha (see col. 4) which contains leucine rich repeats. Thus this protein satisfies the definition of LRR like protein which is a protein that contains leucine rich repeats. Thus the teachings of Miller anticipates the invention of claim 13 as SEQ ID NO 6, taught by Miller, is an amino acid sequence that comprises a 9mer that is identical to amino acids 254-262 of SEQ ID NO 4, amino acids 3-11 of SEQ ID NO 10, and amino acids 236-244 of SEQ ID NO 17.

Conclusion

19. No claims are allowable.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya
Patent examiner
Art Unit 1655
Jehanne Souaya
Nov. 14, 2001